G. Gabel
687051

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FILE COVERS 1947 - 10 Aug 2001 VOL 135 ISS 8
FILE LAST UPDATED: 9 Aug 2001 (20010809/ED)

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=> dis his

     (FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIDS, JICST-EPLUS' ENTERED AT
     12:17:23 ON 10 AUG 2001)
                DEL HIS Y

     FILE 'CAPLUS' ENTERED AT 12:24:22 ON 10 AUG 2001
L1             77 S BUECHLER K?/AU
L2             74 S MCPHERSON P?/AU
L3              7 S L1 AND L2
                  E TROPONIN/CT 5
                  E E3
L4          1242 S E6+ALL/CT

=> e steric hindrance/ct 5
E#   FREQUENCY     AT      TERM
--   ---------     --      ----
E1           0      2      STERIC FACTORS/CT
E2           0      2      STERIC FORCE/CT
E3        3608      9 --> STERIC HINDRANCE/CT
E4           0      4      STERIC HINDRANCE (L) BREDT'S RULE/CT
E5           0      2      STERIC POTENTIAL/CT
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=> e e3+all/ct
E1        2757   BT1  Steric effects/CT
E2        3608     -->  Steric hindrance/CT
                    HN   Valid heading during volume 66 (1967) to present.
E3                  UF   Alpha effect, reactivity/CT
E4                  UF   Molecular structure-property relationship (L)
                         steric/CT
E5                  UF   Steric crowding/CT
E6                  UF   Steric effect (L) hindrance/CT
E7                  UF   Steric retardation/CT
E8          34      NT1  Bredt's rule/CT
E9         788      NT1  Ortho effect/CT
*********  END***

=> s e3+nt,uf
PREFERRED TERMS ARE AVAILABLE FOR '"ALPHA EFFECT, REACTIVITY"'
L5           0 "ALPHA EFFECT, REACTIVITY"+NT,UF/CT  (1 TERM)

=> s e2+nf,uf
THE ESTIMATED SEARCH COST FOR FILE 'CAPLUS' IS 11.84 U.S. DOLLARS
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RELATIONSHIP 'NF' IGNORED
NOT A VALID RELATIONSHIP CODE FOR FIELD 'CT'
L6        3635 "STERIC HINDRANCE"+NF,UF/CT  (6 TERMS)

=> s l4 and l6
L7           0 L4 AND L6

=> fil medl,caplus,biosis,embase,wpids,jicst;s (l4 or ?troponin? or ctni or
ctn1)(10a)(cardiac or infarc? or ?card?)
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
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FIELD CODE - 'AND' OPERATOR ASSUMED 'CTN1)(10A)(CARDIAC'
L8        8634 FILE MEDLINE
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'CTN1)(10A)(CARDIAC'
L9        1955 FILE CAPLUS
'"TROPONIN I"' NOT IN RELATIONSHIP FILE
RELATIONSHIP CODE 'ALL' IGNORED
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'CTN1)(10A)(CARDIAC'
L10       4225 FILE BIOSIS
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'CTN1)(10A)(CARDIAC'
L11       2763 FILE EMBASE
RELATIONSHIP 'ALL' IGNORED
RELATIONSHIPS DO NOT EXIST FOR FIELD 'CT'
L12         55 FILE WPIDS
'"TROPONIN I"' NOT IN RELATIONSHIP FILE
RELATIONSHIP CODE 'ALL' IGNORED
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LEFT TRUNCATION IGNORED FOR '?CARD?' FOR FILE 'JICST-EPLUS'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'CTN1)(10A)(CARDIAC'
L13        341 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L14      17973 (L4 OR ?TROPONIN? OR CTNI OR CTN1)(10A)(CARDIAC OR INFARC? OR
               ?CARD?)
The search profile entered contains terms joined by a proximity
operator which does not work in the specified field.  Some proximity
operators work in specific fields.  For example, an expression such as
'OLEFINS/CS(L)REACTIONS/CS' cannot be searched as entered if the (L)
operator does not apply to the CS field.  In such cases, the system
does the search in the field you have specified, but changes the
proximity operator to 'AND' logic.

To look at the terms, operations, etc., in an L#, enter "DISPLAY
QUERY" followed by the L# at an arrow prompt (=>).  To see this
information for a saved query, enter "ACTIVATE" and the query name,
followed by '/Q' at an arrow prompt.

=> s l14 and (l6 or steric hindrance) and ?assay?
RELATIONSHIP 'NF' IGNORED
NOT A VALID RELATIONSHIP CODE FOR FIELD 'CT'
'"STERIC HINDRANCE"' NOT IN RELATIONSHIP FILE
RELATIONSHIP CODE 'NF,UF' IGNORED
L15           0 FILE MEDLINE
L16           0 FILE CAPLUS
RELATIONSHIP 'NF' IGNORED
NOT A VALID RELATIONSHIP CODE FOR FIELD 'CT'
'"STERIC HINDRANCE"' NOT IN RELATIONSHIP FILE
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RELATIONSHIP CODE 'NF,UF' IGNORED
L17             0 FILE BIOSIS
RELATIONSHIP 'NF' IGNORED
NOT A VALID RELATIONSHIP CODE FOR FIELD 'CT'
PREFERRED TERMS ARE AVAILABLE FOR '"STERIC HINDRANCE"'
L18             0 FILE EMBASE
RELATIONSHIP 'NF,UF' IGNORED
RELATIONSHIPS DO NOT EXIST FOR FIELD 'CT'
L19             0 FILE WPIDS
RELATIONSHIP 'NF' IGNORED
NOT A VALID RELATIONSHIP CODE FOR FIELD 'CT'
LEFT TRUNCATION IGNORED FOR '?ASSAY?' FOR FILE 'JICST-EPLUS'
L20             0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L21             0 L14 AND (L6 OR STERIC HINDRANCE) AND ?ASSAY?
Left truncation is not valid in the specified search field in the
specified file.  The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.

=> s ?troponin? and steric hindrance
L22             4 FILE MEDLINE
L23             6 FILE CAPLUS
L24             4 FILE BIOSIS
L25             4 FILE EMBASE
L26             0 FILE WPIDS
LEFT TRUNCATION IGNORED FOR '?TROPONIN?' FOR FILE 'JICST-EPLUS'
L27             0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L28            18 ?TROPONIN? AND STERIC HINDRANCE
Left truncation is not valid in the specified search field in the
specified file.  The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, the Basic Index.

=> dup rem l28
PROCESSING COMPLETED FOR L28
L29             8 DUP REM L28 (10 DUPLICATES REMOVED)

=> d cbib abs 1-8
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L29 ANSWER 1 OF 8 MEDLINE DUPLICATE 1
95046329 Document Number: 95046329. PubMed ID: 7957921. **Troponin** T is capable of binding dystrophin via a leucine zipper. Pearlman J A; Powaser P A; Elledge S J; Caskey C T. (Department of Cell Biology, Baylor College of Medicine, Houston, Texas 77030.) FEBS LETTERS, (1994 Nov 7) 354 (2) 183-6. Journal code: EUH; 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB Using genetic and physical assays for protein-protein interactions, we identified a fast isoform of **troponin** T that binds to dystrophin. **Troponin** T specifically bound to the first of two highly conserved leucine zipper motifs in the carboxy terminus of dystrophin [1,2]. Single amino acid changes in the zipper predicted to disrupt alpha-helix formation or cause **steric hindrance** abolished this binding. These data support the hypothesis that dystrophin couples the contractile apparatus to the sarcolemma and indicate that leucine zipper mediated protein-protein interactions are functionally important in the cytoskeleton as well as the nucleus.

L29 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2001 ACS
1992:171027 Document No. 116:171027 The binding of myosin to actin regulated by flexibility. Entropy-controlled association. Hummel, Z. (Biophys. Dep., Univ. Med. Sch., Pecs, H-7643, Hung.). J. Theor. Biol., 154(3), 331-4 (English) 1992. CODEN: JTBIAP. ISSN: 0022-5193.

AB Expts. have proved that the binding of Ca2+ to the **troponin** complex loosens the F-actin, which is loosened further by the binding of heavy meromyosin. It is suggested that the widely accepted **steric hindrance** model for the assocn. of actin and myosin may not be the major mechanism in the Ca2+ regulation of striated muscle. It is proposed that the flexibility of the Ca2+-loosened segments of the thin filaments can be appropriated for entropy compensation on binding. One of the main roles of the Ca2+ may be to make the thin filaments flexible enough for this assocn.

L29 ANSWER 3 OF 8 MEDLINE DUPLICATE 2
91100413 Document Number: 91100413. PubMed ID: 2148565. Regulation of binding of subfragment 1 in isolated rigor myofibrils. Swartz D R; Greaser M L; Marsh B B. (University of Wisconsin, Muscle Biology Laboratory, Madison 53706.) JOURNAL OF CELL BIOLOGY, (1990 Dec) 111 (6 Pt 2) 2989-3001. Journal code: HMV; 0375356. ISSN: 0021-9525. Pub. country: United States. Language: English.

AB A **steric-hindrance** model has been used to explain the regulation of muscle contraction by tropomyosin-**troponin** complex. The regulation of binding was studied by microscopic observation of mixtures of fluorescent subfragment 1 (S1) with rigor myofibrils at different actin-to-S1 ratios and in the presence and absence of calcium. Procedures were adapted to protect the critical thiols of S1 before conjugation to thiol-specific fluorochromes, this giving fluorescent S1 with unaltered enzyme activity. S1 binding was greatest in the I band (except at the Z-lines) in the presence of calcium regardless of the [S1].

The patterns in the absence of calcium depended on the actin-to-S1 ratios:

low [S1], binding in the myosin-actin overlap region; intermediate [S1], highest binding at the A-I junction; high [S1], greatest binding in the I-band. The two distinct binding patterns observed at low [S1] were demonstrated by dual-channel fluorescence microscopy when myofibrils were sequentially incubated with fluorescent S1 without calcium followed by a different fluorescent S1 with calcium. These observations support the concept of rigor activation of actin sites. The change in the pattern upon increasing [S1] without calcium demonstrate cooperative interactions along the thin filament. However, these interactions (under the conditions used without calcium) do not appear to extend over greater than 2-3 tropomyosin-**troponin**-7 actin functional units.

L29 ANSWER 4 OF 8 MEDLINE DUPLICATE 3
88242815 Document Number: 88242815. PubMed ID: 3378622. The effect of **troponin** C removal on the Ca2+-sensitive binding of Mg2+ AMPPNP to myofibrils. Johnson R E. (University Department of Biochemistry, University of Arizona, Tucson 85721.) FEBS LETTERS, (1988 May 23) 232 (2) 289-92. Journal code: EUH; 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB It was previously shown that when rabbit skeletal myofibrils are titrated with Mg2+ AMPPNP under conditions that result in the dissociation of cross-bridges from the thin filaments (i.e. 50% ethylene glycol, 0 degrees C), Ca2+-sensitive, biphasic binding is observed. These titrations have been repeated using myofibrils from which the **troponin** C has been selectively removed. The disappearance of both Ca2+ sensitivity and biphasic binding is taken as evidence that the Ca2+ sensitivity is due to Ca2+ binding to **troponin** C and the biphasic binding of Mg2+ AMPPNP observed in intact myofibrils is not due to packing constraints or **steric hindrance**.

L29 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2001 BIOSIS
1985:183647 Document No.: BR29:73643. REMOVAL AND RECOMBINATION OF THE REGULATORY LIGHT CHAINS IN RABBIT SKELETAL MYOSIN AND HYBRIDIZATION WITH SCALLOP REGULATORY EDTA LIGHT CHAINS. HAUSERMANN A; SCHAUB M C; WALZTHONY D; WALLIMANN T. DEP. PHARMACOL., UNIV. ZURICH, SWITZ.. 13TH EUROPEAN CONFERENCE ON MUSCLE AND MOTILITY, GWATT, SWITZERLAND, SEPT. 23-28, 1984. J MUSCLE RES CELL MOTIL. (1985) 6 (1), 73-74. CODEN: JMRMD3. ISSN: 0142-4319. Language: English.

L29 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2001 ACS
1983:554039 Document No. 99:154039 Structure of actin and the thin filament.
O'Brien, E. J.; Couch, J.; Johnson, G. R. P.; Morris, E. P. (Med. Res. Counc. Cell Biophys. Unit, King's Coll., London, UK). Actin: Struct. Funct. Muscle Non-Muscle Cells, Proc. Int. Semin., Int. Congr. Biochem., 12th, Meeting Date 1982, 3-15. Editor(s): Dos Remedios, Cristobal G.; Barden, Julian A. Academic: North Ryde, Australia. (English) 1983. CODEN: 50FOAW.

AB The radial d. distributions of F-actin and of actin plus tropomyosin were calcd. from the equatorial x-ray diffraction patterns of oriented gels of these proteins. The distribution for actin has a large peak at a radius

of 2.1 nm and a smaller one at 1.0 nm. With tropomyosin present, there is an addnl. peak at 3.8 nm. A 3-dimensional reconstruction of actin-tropomyosin, with data derived from electron micrographs of paracrystals, shows a similar radial position for tropomyosin, and also confirms the presence of 2 peaks or domains within the actin monomer. The monomer is considerably elongated; from the mutual orientation of adjacent monomers, the polarity of the structure with respect to the Z-line in muscle was detd. Tropomyosin is attached to the smaller domain of actin, but when **troponin**-I is also present in the complex, there is an azimuthal movement, and tropomyosin is probably located near the large domain. A comparison with the analyses by other authors of thin filaments to which myosin subfragment-1 is attached shows more clearly the tropomyosin location in the decorated structure and indicates that each myosin head may interact simultaneously with both actin strands. The proposed position of tropomyosin in filaments contg. **troponin**-I is at 1 of the interaction sites, suggesting that inhibition of thin filament activity may be assocd. with **steric hindrance** at this site.

L29 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2001 BIOSIS
1982:304394 Document No.: BA74:76874. STUDIES ON COOPERATIVE PROPERTIES OF TROPO MYOSIN ACTIN AND TROPO MYOSIN **TROPONIN** ACTIN COMPLEXES BY THE USE OF N ETHYL MALEIMIDE TREATED AND UNTREATED SPECIES OF MYOSIN SUBFRAGMENT 1. NAGASHIMA H; ASAKURA S. INST. OF MOLECULAR BIOL., FAC. OF SCI., NAGOYA UNIV., NAGOYA 464, JAPAN.. J MOL BIOL, (1982) 155 (4), 409-428. CODEN: JMOBAK. ISSN: 0022-2836. Language: English.
AB When subfragment-1 of rabbit skeletal myosin was extensively modified with N-ethylmaleimide, the protein became strongly associable to actin in the presence of MgATP at low ionic strength, while the ATPase ceased to be activated by actin. Various concentrations of the modified protein were mixed with 10 .mu.mol of pure actin or actin complexed with tropomyosin, and the fraction .beta. of actin saturated with the modified protein in each mixture was determined by an ultracentrifugal method. Unmodified subfragment-1 [0.3 .mu.mol] was then added to the same sets of mixtures as used in the above experiments and the rate of ATP hydrolysis V by unmodified subfragment-1 was determined as a function of .beta.. A biphasic V-.beta. relation was obtained for the tropomyosin-actin complex: when .beta. was increased continuously from zero, the rate first increased substantially, had a maximum value more than 10-fold larger than the initial at .beta. .simeq. 0.3, and finally decreased to zero. The V-.beta. profile for pure actin deviated downwards from a linear relation, showing that there was a weak repulsive interaction between the modified and unmodified subfragment-1 species bound to the actin filament. The occurrence of such a repulsion was interpreted in terms of a steric hinderance model. Assuming that the same kind of repulsion underlay the biphasic V-.beta. relation for the tropomyosin-actin complex, the relation

of V'-.beta. was calculated in an ideal case where it was absent. The result was also biphasic. Regulated actin was studied in the presence and absence of Ca2+ by the same method and obtained biphasic V'-.beta. relations in both cases. The experimental results were analyzed by a 2-state model based on the proposal of Bremel & Weber that, within tropomyosin-actin or the regulated actin complex, n actin monomers undergo off/on transitions as a unit. Interactions between units were ignored to estimate the apparent size n, as well as the equilibrium constant L for the transition in the absence of myosin heads. Within the framework of allosteric theory (Monod et al.,), formulae fit for data analysis were derived, a satisfactory agreement of the experimental and theoretical results was found, and values of n = 11, and L = 37 for the tropomyosin-actin complex, and n = 16, L = 9 for regulated actin in the presence of Ca2+ were found. The parameters in its absence could not be determined separately from the V'-.beta. relation which, however, was well-approximated with a combination of n = 16 and L = 10,000. Tropomyosin-actin complex in the on state activated subfragment-1 ATPase 8-fold more strongly than pure actin, and 2.2-2.6-fold more strongly than regulated actin in the on state. The results are compared with those provided by Greene & Eisenberg, Hill et al. and Trybus & Taylor, and discussed in conjunction with the double helical structure of tropomyosin-actin and regulated actin filaments.

L29 ANSWER 8 OF 8 MEDLINE DUPLICATE 4

76039919 Document Number: 76039919. PubMed ID: 1101950. An immunological approach to the role of the low molecular weight subunits in myosin. II. Interaction of myosin and its subfragments with antibodies to the light chains. Holt J C; Lowey S. BIOCHEMISTRY, (1975 Oct 21) 14 (21) 4609-20. Journal code: A0G; 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB Immunological methods, in parellel with measurement of ATPase activity, have been used to characterize the reactions of antibodies specific for light chains with myosin and its water-soluble proteolytic subfragments, heavy meromyosin (HMM) and subfragment 1 (HMM S-1). Antiserum to the 5,5'-dithiobis(2-nitro-enzoic acid) (DTNB) light chain undergoes a precipitation reaction with all of the enzyme species, in which half of the homologous light chain is selectively dissociated. The results suggest that the incomplete dissociation reflects the way in which the light chain is bound, rather than the existence of two distinct species of DTNB 1.c. Little reaction was observed with antisera to alkali-released light chains, indicating that these components in myosin and the subfragments are either largely buried or else conformationally different from the isolated light chains used as immunogens. None of the antisera produced significant changes in Ca2+- or EDTA-ATPase activities. Moreover, calcium regulation through the **troponin**-tropomyosin system was unaffected by removal of DTNB 1.c. from myosin, as well as from the subfragments. The absolute level of actin-activated ATPase activity was, however, consistently lower in the presence of light chain antisera (or purified IgG and antibody) than in aqueous buffer or nonimmune serum. For both alkali and DTNB 1.c. antisera, this loss in activity seemed to result from **steric hindrance** of actin binding by antibody

bound to undissociated light chain. Experimental conditions which would be expected to weaken such an antigen-antibody interaction, as well as the use of monovalent Fab in place of IgG, decreased the inhibition of activity. Altogether the activity measurements suggest that the light chains, particularly DTNB 1.c., are probably not integral parts of either the hydrolytic or actin-binding sites.

```
=> s buechler k?/au,in;s mcpherson p?/au,in
'IN' IS NOT A VALID FIELD CODE
L30          13 FILE MEDLINE
L31          77 FILE CAPLUS
L32          38 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L33          15 FILE EMBASE
L34          43 FILE WPIDS
L35           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L36         186 BUECHLER K?/AU,IN


'IN' IS NOT A VALID FIELD CODE
L37          61 FILE MEDLINE
L38          74 FILE CAPLUS
L39         119 FILE BIOSIS
'IN' IS NOT A VALID FIELD CODE
L40          56 FILE EMBASE
L41          12 FILE WPIDS
L42           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L43         322 MCPHERSON P?/AU,IN

=> s l36 and l43
L44           2 FILE MEDLINE
L45           7 FILE CAPLUS
L46           9 FILE BIOSIS
L47           2 FILE EMBASE
L48           7 FILE WPIDS
L49           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L50          27 L36 AND L43

=> s l50 not l28
L51           2 FILE MEDLINE
L52           7 FILE CAPLUS
L53           9 FILE BIOSIS
L54           2 FILE EMBASE
L55           7 FILE WPIDS
L56           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
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L57 27 L50 NOT L28

=> dup rem l57
PROCESSING COMPLETED FOR L57
L58 18 DUP REM L57 (9 DUPLICATES REMOVED)

=> d 1-18 cbib abs

L58 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2001 ACS
2001:43458 Document No. 134:97519 Methods for the assay of troponin I and T and complexes of troponin I and T and selection of antibodies for use in immunoassays. **Buechler, Kenneth F.**; Mcpherson, Paul H. (Biosite Diagnostics, Inc., USA). U.S. US 6174686 B1 20010116, 39 pp., Cont.-in-part of U.S. 5,795,725. (English). CODEN: USXXAM.
APPLICATION:
US 1996-633248 19960418. PRIORITY: US 1995-423582 19950418.
AB Assay systems and specialized antibodies are disclosed for the detection and quantitation of troponin I and troponin T in body fluids as an indicator of myocardial infarction. Since troponin I and T exist in various conformations in the blood, the ratios of the monomeric troponin I
an T and the binary and ternary complexes, as well as which form of troponin present in the blood, may be related to the metabolic state of the heart. Disclosed is a system to det. the presence of a troponin form or a group of troponin forms in a sample of whole blood, serum or plasma. Disclosed is a stabilized compn. of troponin; the stabilized compn. can comprise a stabilized compn. of troponin I, wherein the troponin I is oxidized, the troponin I can be unbound or the troponin I can be in a complex. Disclosed is a method for improving the recovery of troponin I or T from a surface used in immunoassays. Also disclosed are antibodies which recognize unbound troponin forms, the forms of troponin in binary complexes, the ternary complex of troponin I, T and C, and the conformations of troponin I having intramolecularly oxidized and reduced cysteines.

L58 ANSWER 2 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
2001:378375 Document No.: PREV200100378375. Methods for monitoring the status of assays and immunoassays. **Buechler, Kenneth F.**; Anderberg, Joseph M. (1); **McPherson, Paul H.**. (1) Encinitas, CA USA.
ASSIGNEE: Biosite Diagnostics, Inc.. Patent Info.: US 6194222 February 27,
2001. Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 27, 2001) Vol. 1243, No. 4, pp. No Pagination. e-file. ISSN: 0098-1133. Language: English.
AB The invention relates in part to the use of independent assay controls (IACs) for the optical communication between an assay device and an instrument in monitoring and performing assays, preferably immunoassays.

L58 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2001 ACS
2001:197302 Microfluidics in Triage- lab chips: A new dimension to immunoassays. **Buechler, Kenneth F.**; **McPherson, Paul H.**; Lesefko, Steve; Nakamura, Kevin (Research and Development, Biosite, San Diego, CA, 92121, USA). Abstr. Pap. - Am. Chem. Soc., 221st, ANYL-215 (English) 2001. CODEN: ACSRAL. ISSN: 0065-7727. Publisher: American Chemical Society.

AB The Triage Lab Chip performs multiple, independent immunoassays in 15 min to measure targets in biol. fluids. Blood or other biol. fluid is added to the Lab Chip and a filter on the Lab Chip separates red blood cells from the plasma or other insol. matter from the fluid. Surface architecture and relative hydrophobicity of microcapillaries control microfluidics in the Lab Chip. Precise microcapillaries (15.mu.m to 250.mu.m) are formed by the assembly of plastic lids and bases. The edges of the microcapillaries are made hydrophobic to prevent accelerated flow at capillary junctions. Hydrophobic surfaces are used to impede flow within microcapillaries to provide incubation of the sample and fluorescent antibodies. Structures within the microcapillaries allow fluid to move from high to low capillarity. The Lab Chip comprises a protein array microcapillary contg. antibodies for capture of fluorescent antibody-target complexes. Target concns. are detd. from the fluorescence of the captured fluorescent antibody-target complexes at the surface of the Lab Chip. Fluorescence is measured in 2 min by a portable fluorometer called the Triage Meter. The Lab Chips currently on the market are the Triage Cardiac Panel and Triage BNP Test, which aid in the diagnosis of myocardial infarction and congestive heart failure, resp. Details of the surface architecture, the microfluidics and performance of the Triage Lab Chips will be discussed.

L58 ANSWER 4 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
2001:279875 Document No.: PREV200100279875. Microfluidics in Triage(R) Lab Chips: A new dimension to immunoassays. **Buechler, Kenneth F. (1)** ; **McPherson, Paul H. (1)**; Lesefko, Steve (1); Nakamura, Kevin (1). (1) Research and Development, Biosite, 11030 Roselle St., San Diego, CA, 92121: kbuechler@biosite.com USA. Abstracts of Papers American Chemical Society, (2001) Vol. 221, No. 1-2, pp. ANYL 215. print. Meeting Info.: 221st National Meeting of the American Chemical Society San Diego, California, USA April 01-05, 2001 ISSN: 0065-7727. Language: English. Summary Language: English.

L58 ANSWER 5 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
2001:283472 Document No.: PREV200100283472. Methods for the recovery and measurement of troponin complexes. **Buechler, Kenneth F.**; **McPherson, Paul H. (1)**. (1) Encinitas, CA USA. ASSIGNEE: Biosite Diagnostics, Inc.. Patent Info.: US 6156521 December 05, 2000. Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 5, 2000) Vol. 1241, No. 1, pp. No Pagination. e-file. ISSN: 0098-1133. Language: English.
AB The invention relates in part to methods and compositions for identifying the presence, measuring the amount, stabilizing, and facilitating recovery of troponin complexes or individual troponin isoforms in a sample.

L58 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
1999:454283 Document No. 131:85160 Methods for monitoring the status of assays. **Buechler, Kenneth F.**; Anderberg, Joseph M.; McPherson, Paul H. (Biosite Diagnostics, Inc., USA). PCT Int. Appl. WO 9935602 A1 19990715, 149 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG,

BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US261 19990104. PRIORITY: US 1998-3065 19980105.

AB The invention relates in part to the use of independent assay controls (IACs) for the optical communication between an assay device and an instrument in monitoring and performing assays, preferably immunoassays. Prepn. of fluorescent energy transfer latex with bovine serum albumin and antibody conjugates and their application in cardiac marker detn. are described.

L58 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2

1999:425815 Document No. 131:56141 Methods for the recovery and measurement of troponin complexes for detecting myocardial infarction. **Buechler, Kenneth F.**; Mcpherson, Paul H. (Biosite Diagnostics, Inc., USA). PCT Int. Appl. WO 9932888 A1 19990701, 119 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US26986 19981218. PRIORITY: US 1996-769077 19961218; US 1997-993750 19971219.

AB The invention relates in part to methods and compns. for identifying the presence, measuring the amt., stabilizing, and facilitating recovery of troponin complexes or individual troponin isoforms in a sample. Alk. phosphatase was conjugated with anti-troponin antibodies and biotinylated troponin antibodies and avidin-HS magnetic latex particles were prepd. for use in troponin ELISA immunoassays. Troponins I and T were detected in human serum, plasma, and solns.

L58 ANSWER 8 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3

1999:515905 Document No.: PREV199900515905. Diagnostic for determining the time of a heart attack. **Buechler, Kenneth Francis (1)**; **McPherson, Paul H.**. (1) Department of Physics/Biophysics, University of California, San Diego, San Diego, CA USA. ASSIGNEE: Biosite Diagnostics Incorporated. Patent Info.: US 5947124 Sep. 07, 1999. Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 7, 1999) Vol. 1226, No. 1, pp. NO PAGINATION. ISSN: 0098-1133. Language: English.

L58 ANSWER 9 OF 18 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1999-458352 [38] WPIDS

AB WO 9935718 A UPAB: 19990922

NOVELTY - A ROM chip carrier (1200) for use in an assay device has a chip cavity and a leading edge (1212) with teeth having one of their dimensions

defined by the width of the edge.
USE - The ROM chip carrier is useful in the automated fluorometry of samples of blood, serum, plasma, urine, faecal extract, water, soil extract, chemicals, etc.
DESCRIPTION OF DRAWING(S) - The diagram shows an example implementation of a chip carrier.
ROM chip carrier 1200
cross member 1207
leading edge 1212
top face 1204
lateral membrane 1206
tab 1234
chip cavity 1236
recess 1237.
Dwg.12B/16

L58 ANSWER 10 OF 18 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-458321 [38] WPIDS
AB WO 9935486 A UPAB: 19990922
NOVELTY - A fluorometer has a processor controlling the operation of a test performed by an assay device on a sample. A removable storage medium accepts one of several removable media, each of which includes datasets for assay(s) to be performed.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) a method of performing testing in a sample comprises using the fluorometer;
(2) a computer readable medium stores an executable sequence for optically exciting an assay device and detecting the resulting emitted energy;
(3) a fluorometer performing a sequence as in (2);
(4) a computer readable medium stores an executable sequence including accepting an assay device, reading its encoded label in order to determine the test that is to be performed on it;
(5) a fluorometer including the preceding aspects and the medium is a ROM chip carrier;
(6) a test instrument for assaying a patient sample at home has a communications interface for either receiving instructions from a remote database on a test to be performed and/or sending the results to a remote healthcare facility.
USE - Immunoassay fluorometer for home use to analyze biological samples.
DESCRIPTION OF DRAWING(S) - The figure shows a functional fluorometer.
processor 104
power supply 108
user interface 112
memory 116
COMM interface 120
assay device 122
assay mechanism 124
storage 128
socket 132

ROM chip 136
keypad 162
display 164
printer 166
Dwg.1/16

L58 ANSWER 11 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
1999:536366 Document No.: PREV199900536366. Triage(R) point of care quantitative immunoassay system. **Buechler, Kenneth F. (1); McPherson, Paul**; Anderberg, Joseph; Lesefko, Stephen; Nakamura, K.; Briggs, Jason; Rongey, Scott. (1) Biosite Diagnostics Inc., 11030 Roselle Street, San Diego, CA, 92121 USA. Journal of Clinical Ligand Assay, (Summer, 1999) Vol. 22, No. 2, pp. 208-213. ISSN: 1081-1672. Language: English. Summary Language: English.

AB We have developed an immunoassay system that quantifies in about 15 minutes the concentration of a single or multiple analytes in biological fluids. The Triage(R) Cardiac Panel measures simultaneously the concentrations from whole blood of CKMB, troponin I (TnI), and myoglobin. The technology also allows the measurement of cyclosporin concentration, in which lysed whole blood is used. The test procedure involves addition of several drops of blood to a small disposable assay device. The assay device incorporates novel concepts of capillarity and defined surface architectures to drive and control fluid flow during the immunoassay. After addition of sample to the device, the device is inserted into a small portable instrument, which determines assay completion and the analyte concentrations. The concentrations of the analytes are calculated from calibration curves downloaded from an EEprom. The technical and performance aspects of the product will be discussed.

L58 ANSWER 12 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
1999:461541 Document No.: PREV199900461541. A rapid, quantitative point of care assay system for the simultaneous measurement of CKMB, Troponin I and Myoglobin in blood. **Buechler, K. F. (1); Mcpherson, P. H. (1)**; Anderberg, J. M. (1); Lesefko, S. M.; Fiechtner, M. D. (1); Sundquist, A. R. (1); Dwyer, B. P. (1); Nakamura, K. K. (1); Buechler, J. A.. (1) Research, Biosite Diagnostics, Inc., San Diego, CA USA. Clinical Chemistry and Laboratory Medicine, (June, 1999) Vol. 37, No. SPEC. SUPPL., pp. S82. Meeting Info.: IFC-WorldLab, International Federation of Clinical and Laboratory Medicine (17th International and 13th European Congress of Clinical Chemistry and Laboratory Medicine, 1st International Congress of Clinical Molecular Biology, 31st National Congress of the Italian Society of Clinical Biochemistry and Clinical Molecular Biology) Florence, Italy June 6-11, 1999 International Federation of Clinical and Laboratory Medicine. ISSN: 1434-6621. Language: English.

L58 ANSWER 13 OF 18 MEDLINE
1999416632 Document Number: 99416632. PubMed ID: 10558304. A STAT cardiac marker system for detecting acute heart attacks. Bruni J; **McPherson P; Buechler K.** (Clinical and Regulatory Affairs, Biosite Diagnostics, Inc., San Diego, CA 92121, USA.. jbruni@biosite.com) . AMERICAN CLINICAL LABORATORY, (1999 Aug) 18 (7) 14-6. Journal code: BCC;

8903666. ISSN: 8750-9490. Pub. country: United States. Language: English.

L58 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 5
1998:424405 Document No. 129:38405 Method for improving the recovery of troponin I and T. **Buechler, Kenneth F.**; McPherson, Paul H. (Biosite Diagnostics, Inc., USA). PCT Int. Appl. WO 9827435 A1 19980625, 117 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US23252 19971215. PRIORITY: US 1996-769077 19961218.
AB A method to facilitate recovery troponin I and/or troponin T from a sample comprising addn. of troponin C to the sample or to a surface from which the troponin I and/or troponin T are recovered.

L58 ANSWER 15 OF 18 MEDLINE DUPLICATE 6
1998286707 Document Number: 98286707. PubMed ID: 9625043.
Characterization of cardiac troponin subunit release into serum after acute myocardial infarction and comparison of assays for troponin T and I.
American Association for Clinical Chemistry Subcommittee on cTnI Standardization. Wu A H; Feng Y J; Moore R; Apple F S; **McPherson P H; Buechler K F**; Bodor G. (Department of Pathology, Hartford Hospital, CT 06102, USA.. awu@harthosp.org) . CLINICAL CHEMISTRY, (1998 Jun) 44 (6 Pt 1) 1198-208. Journal code: DBZ; 9421549. ISSN: 0009-9147. Pub. country: United States. Language: English.
AB We examined the release of cardiac troponin T (cTnT) and I (cTnI) into the blood of patients after acute myocardial infarction (AMI). Three postAMI serum samples were applied in separate analytical runs onto a calibrated gel filtration column (Sephacryl S-200), and the proteins were separated by molecular weight. Using commercial cTnT and cTnI assays measured on collected fractions, we found that troponin was released into blood as a ternary complex of cTnT-I-C, a binary complex of cTnI-C, and free cTnT, with no free cTnI within the limits of the analytical methodologies. The serum samples were also examined after incubation with EDTA and heparin. EDTA broke up troponin complexes into individual subunits, whereas heparin had no effect on the assays tested. We added free cTnC subunits to 24 AMI serum samples and found no marked increase in the total cTnI concentrations, using an immunoassay that gave higher values for the cTnI-C complex than free cTnI. To characterize the cross-reactivity of cTnT and cTnI assays, purified troponin standards in nine different forms were prepared, added to serum and plasma pools, and tested in nine quantitative commercial and pre-market assays for cTnI and one approved assay for cTnT. All nine cTnI assays recognized each of the troponin I forms (complexed and free). In five of these assays, the relative responses for cTnI were nearly equimolar. For the remainder, the response was substantially greater for complexed cTnI than for free cTnI. Moreover,

there was a substantial difference in the absolute concentration of results between cTnI assays. The commercial cTnT assay recognized binary and ternary complexes of troponin on a near equimolar basis. We conclude that all assays are useful for detection of cardiac injury. However, there are differences in absolute cTnI results due to a lack of mass standardization and heterogeneity in the cross-reactivities of antibodies to various troponin I forms.

L58 ANSWER 16 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
1998:339897 Document No.: PREV199800339897. A rapid, quantitative point-of-care assay system for simultaneous measurement of CKMB, troponin I and myoglobin in blood. **McPherson, P. H.**; Anderberg, J. M.; Lesefko, S. M.; Fiechtner, M. D.; Sundquist, A. R.; Dwyer, B. P.; Nakamura, K. K.; Bruni, J. F.; **Buechler, K. F.**; et al.. Biosite Diagnostics Inc., 11030 Roselle St., San Diego, CA 92121 USA. Clinical Chemistry, (June, 1998) Vol. 44, No. 6 PART 2, pp. A116. Meeting Info.: 50th Annual Meeting of the American Association of Clinical Chemistry Chicago, Illinois, USA August 2-6, 1998 ISSN: 0009-9147. Language: English.

L58 ANSWER 17 OF 18 BIOSIS COPYRIGHT 2001 BIOSIS
1997:334418 Document No.: PREV199799633621. Characterization and measurement of troponin I, troponin T and troponin complexes in blood from AMI patients. **McPherson, P. H.**; **Buechler, K. F.**. Biosite Diagnostics, San Diego, CA USA. Clinical Chemistry, (1997) Vol. 43, No. 6 PART 2, pp. S136. Meeting Info.: 49th Annual Meeting of the American Association for Clinical Chemistry Atlanta, Georgia, USA July 20-24, 1997 ISSN: 0009-9147. Language: English.

L58 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 7
1996:732033 Document No. 126:4213 Novel methods for the assay of troponin I and T and complexes of troponin I and T and selection of antibodies for use in immunoassays. **Buechler, Kenneth F.**; Mcpherson, Paul H. (Biosite Diagnostics Incorporated, USA). PCT Int. Appl. WO 9633415 A1 19961024, 139 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US5476 19960418. PRIORITY: US 1995-423582 19950418.

AB Disclosed is a system to det. the presence of a troponin form or a group of troponin forms in a sample of whole blood, serum or plasma. Disclosed is a stabilized compn. of troponin; the stabilized compn. can comprise a stabilized compn. of troponin I, wherein the troponin I is oxidized, the troponin I can be unbound or the troponin I can be in a complex. Disclosed is a method for improving the recovery of troponin I or T from a surface used in immunoassays. Also disclosed are antibodies which recognize, unbound troponin forms, the forms of troponin in binary complexes, the ternary complex of troponin I, T and C, and the conformations of troponin I having intramolecularly oxidized and reduced cysteines.